APPENDIX II

CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS PURSUANT TO 37 C.F.R. § 1.121 (c)(3)

42. A method of constructing a population of altered heavy chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor heavy chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor heavy chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified heavy chain variable region framework region, or portion thereof, wherein said heavy chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or portion thereof, wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered heavy chain variable region encoding nucleic acids is constructed.

43. The method of Claim 42, wherein said representation of first and second reference sequences is in electronic form.

44. The method of Claim 42, further comprising the step of (e) coexpressing said population of altered heavy chain variable region encoding nucleic acids with a light chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

45. The method of Claim 42, wherein said synthesizing comprises chemically synthesizing.

46. The method of Claim 42, wherein said acceptor is human.

47. A method of constructing a population of altered light chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor light chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor light chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified light chain variable region framework region, or portion thereof, wherein said light chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or portion thereof,

wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered light chain variable region encoding nucleic acids is constructed.

48. The method of Claim 47, wherein said representation of first and second reference sequences is in electronic form.

49. The method of Claim 47, further comprising the step of (e) coexpressing said population of altered light chain variable region encoding nucleic acids with a heavy chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

50. The method of Claim 47, wherein said synthesizing comprises chemically synthesizing.

51. The method of Claim 47, wherein said acceptor is human.

52. A method of constructing a population of altered heavy chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor heavy chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor heavy chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified heavy chain variable region framework region, or portion thereof, wherein said heavy chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or portion thereof, wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) extending said overlapping oligonucleotides with a DNA polymerase under conditions such that a population of altered heavy chain variable region encoding nucleic acids is constructed.

53. The method of Claim 52, wherein said representation of first and second reference sequences is in electronic form.

54. The method of Claim 52, further comprising the step of (e) coexpressing said population of altered heavy chain variable region encoding nucleic acids with a light chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

55. The method of Claim 52, wherein said synthesizing comprises chemically synthesizing.

56. The method of Claim 52, wherein said acceptor is human.

57. A method of constructing a population of altered light chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor light chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor light chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified light chain variable region framework region, or portion thereof, wherein said light chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or portion thereof, wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) extending said overlapping oligonucleotides with a DNA polymerase under conditions such that a population of altered light chain variable region encoding nucleic acids is constructed.

58. The method of Claim 57, wherein said representation of first and second reference sequences is in electronic form.

59. The method of Claim 57, further comprising the step of (e) coexpressing said population of altered light chain variable region encoding nucleic acids with a heavy chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

60. The method of Claim 57, wherein said synthesizing comprises chemically synthesizing.

61. The method of Claim 57, wherein said acceptor is human.

62. A method of constructing a population of altered heavy chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor heavy chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and Chothia; said second reference amino acid sequence comprising the sequence of an acceptor heavy chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified heavy chain variable region framework region, or portion thereof, wherein said heavy chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence, and wherein said changed amino acids were introduced through the use of codon-based mutagenesis; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or

portion thereof, wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and wherein said different amino acid was introduced through the use of codon-based mutagenesis, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered heavy chain variable region encoding nucleic acids is constructed.

63. The method of Claim 62, wherein said representation of first and second reference sequences is in electronic form.

64. The method of Claim 62, further comprising the step of (e) coexpressing said population of altered heavy chain variable region encoding nucleic acids with a light chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

65. The method of Claim 62, wherein said synthesizing comprises chemically synthesizing.

66. The method of Claim 62, wherein said acceptor is human.

67. A method of constructing a population of altered light chain variable region encoding nucleic acids, comprising:

a) providing a representation of first and second reference amino acid sequences, said first reference amino acid sequence comprising the sequence of a donor light chain variable region, said donor variable region comprising i) framework regions and ii) three complementarity-determining regions as defined by the combined definitions of Kabat and

Chothia; said second reference amino acid sequence comprising the sequence of an acceptor light chain variable region comprising framework regions;

b) synthesizing i) a first population of oligonucleotides, comprising oligonucleotides encoding a modified light chain variable region framework region, or portion thereof, wherein said light chain variable region framework region, or portion thereof, contains a plurality of changed amino acids at one or more positions when compared to said acceptor framework region reference sequence, wherein said framework positions that are changed are selected from among said acceptor framework positions of said second reference sequence that differ at the corresponding position compared to the donor framework positions of said first reference sequence, and wherein said changed amino acids were introduced through the use of codon-based mutagenesis; and ii) a second population of oligonucleotides, each encoding at least one modified complementarity-determining region, or portion thereof, wherein said modified complementarity-determining region, or portion thereof, comprises a different amino acid at one or more positions when compared to the corresponding donor complementarity-determining region amino acid reference sequence, and wherein said different amino acid was introduced through the use of codon-based mutagenesis, and one or more portions of adjacent framework regions which are capable of hybridizing to said first population of oligonucleotides; and

c) mixing said first and second populations of oligonucleotides so as to create overlapping oligonucleotides; and

d) treating said overlapping oligonucleotides under conditions such that a population of altered light chain variable region encoding nucleic acids is constructed.

68. The method of Claim 67, wherein said representation of first and second reference sequences is in electronic form.

69. The method of Claim 67, further comprising the step of (e) coexpressing said population of altered light chain variable region encoding nucleic acids with a heavy chain variable region encoding nucleic acid so as to produce a diverse population of altered heteromeric variable regions.

70. The method of Claim 67, wherein said synthesizing comprises chemically synthesizing.

71. The method of Claim 67, wherein said acceptor is human.